



## Targeting population heterogeneity in *Saccharomyces cerevisiae* batch fermentation for optimal cell factories

Heins, Anna-Lena; Lencastre Fernandes, Rita; Lundin, L.; Carlqvist, Magnus; Sørensen, S.; Gernaey, Krist; Eliasson Lantz, Anna

*Publication date:*  
2011

[Link back to DTU Orbit](#)

### *Citation (APA):*

Heins, A-L., Lencastre Fernandes, R., Lundin, L., Carlqvist, M., Sørensen, S., Gernaey, K., & Eliasson Lantz, A. (2011). *Targeting population heterogeneity in Saccharomyces cerevisiae batch fermentation for optimal cell factories*. Abstract from 6th Danish Conference on Biotechnology and Molecular Biology, Vejle, Denmark. <http://www.biokemi.org/meetings/56>

---

### General rights

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the public portal

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

# Targeting population heterogeneity in *Saccharomyces cerevisiae* batch fermentation for optimal cell factories

Heins A.L.<sup>1\*</sup>, Lencastre Fernandes R.<sup>2</sup>, Lundin, L.<sup>3</sup>, Carlquist M.<sup>4</sup>, Sörensen S.<sup>3</sup>, Gernaey V.K.<sup>2</sup>, Eliasson Lantz A.<sup>1</sup>

<sup>1</sup>Center for Microbial Biotechnology, Technical University of Denmark, Denmark

<sup>2</sup>Department of Chemical and Biochemical Engineering, Technical University of Denmark, Kgs. Lyngby, Denmark

<sup>3</sup>Department of Biology, University of Copenhagen, Copenhagen, Denmark

<sup>4</sup>Department of Chemistry, Lund University, Lund, Sweden

\*anlh@bio.dtu.dk

To achieve an efficient production process, it is essential to optimize both the strain and the cultivation conditions. Traditionally, a microbial population has been considered homogeneous in optimization studies of fermentation processes. However, research has shown that a typical microbial population in a fermentor is heterogeneous. There are indications that such heterogeneity may be both beneficial (facilitates quick adaptation to new conditions) and harmful (reduces yields and productivities) for the robustness of the fermentation process (Bylund *et al.* (1998); Enfors *et al.* (2001)). Significant gradients of e.g. dissolved oxygen, substrates, and pH are typically observed in many industrial scale fermentation processes. Consequently, the microbial cells experience rapid changes in environmental conditions as they circulate throughout the reactor, which might pose stress on the cells and affect their metabolism and consequently affect the heterogeneity level of the population.

To further investigate these phenomena and gain a deeper understanding of population heterogeneity, *Saccharomyces cerevisiae* growth reporter strains based on the expression of green fluorescent protein (GFP) were constructed which enabled us to perform single cell level analysis, and thereby created the possibility to map population heterogeneity. A factorial design with pH, glucose concentration and oxygen level was performed in batch cultivations using the growth reporter strains to evaluate the effect of those environmental factors on heterogeneity level and amount of living cells.

A highly dynamic behavior with regard to subpopulation distribution during the different growth stages was seen for the batch cultivations. Moreover, it could be demonstrated that the glucose concentration had a clear influence on the heterogeneity. The results from the factorial design experiments will be further discussed.

## References

Bylund F, Collet E, Enfors S, Larsson G. Substrate gradient formation in the large-scale bioreactor lowers cell yield and increases by-product formation. *Bioprocess Biosyst Eng.* 1998; 18:171-180.

Enfors SO, Jahic M, Rozkov A, Xu B, Hecker M, Jürgen B, Krüger E, Schweder T, Hamer G, O'Beirne D, Noisommit-Rizzi N, Reuss M, Boone L, Hewitt C, McFarlane C, Nienow A, Kovacs T, Trägårdh C, Fuchs L, Revstedt J, Friberg PC, Hjertager B, Blomsten G, Skogman H, Hjort S, Hoeks F, Lin HY, Neubauer P, van der Lans R, Luyben K, Vrabel P, Manelius A. Physiological responses to mixing in large scale bioreactors. *J Biotechnol* 2001; 85:175-185